

IN THE SPECIFICATION

(1) On page 1, please delete the first paragraph after the title and replace with the following paragraph:

This application is a divisional of application Serial No. 09/754,066, filed January 5, 2001, which is a continuation of application Serial No. 08/848,013, filed April 28, 1997, which is a continuation-in-part of application Serial No. 08/185,416, filed January 24, 1994, which is a continuation-in-part of application Serial No. 08/002,395, filed January 13, 1993, which is a continuation-in-part of application Serial No. 07/748,277, filed August 21, 1991, and application Serial No. 07/830,886, filed February 4, 1992 which is a continuation-in-part of application Serial No. 07/815,130, filed December 27, 1991.

(2) Delete the paragraph bridging pages 2 and 3 and replace it with the following paragraph:

Bracht et al., (Biochem. and Biophys. Res. Com., vol. 200, No.2, 1994, pp.933-937) have disclosed four aptamer sequences derived from the unfractionated defibrotide DNA precursor molecule. Two aptamers (5'-GGTTGGATTGGTTGG-3' (SEQ ID NO:1) and 5'-GGTTGGATCGGTTGG-3' (SEQ ID NO:2)) were identified by thrombin chromatography. Another aptamer (5'-GGATGGATCGGTTGG-3' (SEQ ID NO:3)) was found in the PCR product from the double-stranded DNA precursor. The sequence of such aptamer was used to search the EMBL data base and was found in the bovine genome and Angiotensin II-AT1 receptor. The three aptamers were found to have inhibitory activities of thrombin induced platelet aggregation, thromboxane biosynthesis, increase in cytosolic Ca ++, and fibrin clot formation. In addition, there is a non-function

apatamer (5'-GGTGGTGGTTGTGGT3' (SEQ ID NO:4)) which did not display any of the activities characteristic of defibrotide.

(3) On page 19 delete the paragraph beginning of line 15 and replace it with the following paragraph:

The homology level may be at least from about 50% to about 70%, preferably 80% to 90%, more preferably 95%. The homologous region may be continuous or scattered through out a nucleotide fragment. For example, aptamer #1 of defibrotide (5'-GGTTGGATTGGTTGG-3' (SEQ ID NO:1)) has complete and partial homology to several genomes, *e.g.*, Schizosaccharomyces, pombe GATA-binding region, and Streptococcus pneumonia Dpn I gene. Aptamer #2 of defibrotide (5'-GGTTGGATCGGTTGG-3' (SEQ ID NO:2)) has homology to several genomes, *e.g.*, Mycobacterium leprae cosmid B0462.

(4) On page 20 delete the paragraph beginning on line 1 and replace with the following paragraph:

Aptamer #4 of defibrotide (5'-GGTGGTGGTTGTGGT-3' (SEQ ID NO:4)) has homology to various genomes, *e.g.*, chicken liver cell adhesion molecule, human gelatin receptor mRNA, Schistosoma japonicum eggshell protein, Schistosoma japonicum ESG-1 protein mRNA, human mRNA with TGG repeat clone 83, Schistosoma japonicum ESG-2AA protein mRNA, Candida tropicalis POX9 gene, Candida Tropicalis cat gene, Schistocerca americana Antennapedia, chicken liver cell adhesion molecule, human papilloma virus type 20, homo sapiens mitochondrial genome, gorilla mtDNA, human

mtDNA, human DNA sequence from cosmid U157D, Leishmania major cosmid clone L2759, Plasmodium vivax Serine repeat antigen, P. clarkii mRNA, Trypanosoma cruzi mucin-like protein, L. major mRNA for surface antigen P2, Aspergillus aculeatus (clone PC1G1), Candida Albicans DNA for MNT2 gene, E. Coli K-12 genome, Mouse amyloid beta precursor, Candida Albicans topoisomerase type, human homolog of Drosophila splicing gene, E. Coli gcvh gene 3' end, human Down Syndrome region of Chromosome, E. Coli gcv operon gene sequence, Drosophila melanogaster receptor protein and polyheamotic DNA, human Papilloma virus type 25 genomic, Drosophila melanogaster Zn finger, Pneumocystis carinii, Dystrophin associated protein of Duchenne's muscular drstrophy, (Sequence 7 from US # 5,449,616), and DNA Polymerase (Sequence 14 from US # 5,556,772).

(5) Delete the paragraph bridging pages 20 and 21 and replace it with the following paragraph:

Variants of apatamer #4 also include homologous sequences of HIV and apatamer #4. For example, homologous sequences may be found in gag/pol, c-vif, or env regions of HIV. Particular homologous sequences may be found on three sites on gag/pol HIV genome region. The translation of the apatamer #4 region on gag site is a peptide 'PEPTA', and the pol gene fragment translates the same DNA sequence into 'TRANS. In a preferred embodiment, S-Oligo variants of apatamer #4 are 1) 5'GGGCTGTTGGCTCTGGTCTGCTCTGAAGGAAATTCCTGGCCTTCCCTTG3' (SEQ ID NO:15), 2) 5'ACCAGAGCCAACAGC3' (SEQ ID NO:16), 3) 5'CCTGGCCTTCCCTTG3' (SEQ ID NO:17).

(6) Delete table on page 26 and replace with the following table:

Oligonucleotide	<u>SEQ ID</u> <u>NO:</u>	Homology Region in HIV	Cellular Regulatory Factor
CAGCTGCACCTGCCAAG C	<u>5</u>	gag/pol 968-984	human TNF receptor
ATAAAATATACCATATA CA	<u>6</u>	gag 2315-2331	human RIP protein kinase (HSU50062)
TCATAAAATATACTATA TTCA	<u>7</u>	gag 2312-2331	mouse TNF receptor (mmu 25995)
ATATTAAAGAACGCTGT TTACAATACTTGG	<u>8</u>	vif 4847-4876	IL-2 receptor
ATGCAGTTGTGAAGAGA A	<u>9</u>	env 7485-7502	TNF receptor (cell death protein HSU25994)
AATTAAGGCATAAGAA AACTAAGAAATATGCAC	<u>10</u>	env 6118-6150	IL-1 analog
TCTCTCCCTCAAGGACT CAGCTTTCTGAAG	<u>11</u>	5' untranslated region pos. 60-90	TNF- α promoter
CAATAATAAAAGGGGA AA	<u>12</u>	gag 186-203	c-myc
AGTGCAACCGGCAGGA GGTGA	<u>13</u>	5' untranslated region pos. 88-109	c-abl
GCCACCAGCCCCTCCCC AGACTCTCAGGTGGAGG CAACAG	<u>14</u>	pol 1522-1547	B-myb, c-myc protooncogene

(7) Delete the paragraph bridging pages 29 and 30 and replace with the following paragraph:

In replication/expression vectors, the oligonucleotides of the present invention can

be flanked by some buffer sequences. In a preferred embodiment, pCI-neo vector can be cut by Bgl2 and BamH1, and eIF-4E initiation factor gene may be inserted. The sequence of eIF-4E gene specificity relevant to such vector is GGCCAGGCATGGTAAGTCATACCTATAATCCCAGCACTGTGGGAGGCCAAGG AAGGGGGATCCCTTGAGCTCAAGAGTTTAAGACCGAGATCGAT (SEQ ID NO:18) (upstream of Alu) and AAGAGTTTAAGACCAGCTTGGGCAACACAGT CAGACTTCATCTCTATAAATAATTTAAAAATTAGCCAAGCATGGTGGCGTGGT ACCCTTGTGGGTTCCAGGCTTATTTGGGAGGTTGAGGTAAAGGAATTCTCTTG GACGCCCAGGTAGTCAAGGTTGCAGTGAGCCATAATCAAACCACTGCACTCC AGCATGGCAACAGAGCAAGACCCATCTCAATATAT (SEQ ID NO:19) (downstream of Alu). Subsequently, the oligonucleotides of the present invention can be inserted into the eIF-4E gene, preferably at the Alu site of eIF-4E gene.

(8) Please insert the sequence listing in the application after the Abstract and before the Figures.

Date:

Feb 2, 2004

Respectfully submitted,

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